

Bowel Urgency in Inflammatory Bowel Disease

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Abstract

Inflammatory bowel disease (IBD) significantly impacts the patient's quality of life with chronic disabling symptoms such as diarrhea, abdominal pain, bowel urgency, weight loss, fatigue.

Bowel urgency, the sudden or immediate need for a bowel movement, is distinct from increased stool frequency and its underlying mechanisms are multifactorial and may vary within and between patients being driven primarily by active inflammation. It is one of the most bothersome symptoms experienced by patients with ulcerative colitis, with substantial negative impacts on quality of life and psychosocial functioning.

Bowel urgency is often not discussed by patients due to embarrassment, and it may not be addressed adequately by healthcare providers. In fact, patients may report bowel urgency even if they are considered in remission based on symptoms or endoscopic findings. Several patient's reported outcomes tools have been developed to measure the impact of urgency on patients' life.

This article presents the main challenges related to integration of bowel urgency into current care of IBD patients and its impact on treatment choice and monitoring.

Key words: bowel urgency, ulcerative colitis, Crohn's disease, patient reported outcomes, treatment targets, quality of life, IBD

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INTRODUCTION

Inflammatory bowel disease (IBD) is characterized by chronic inflammation with flare-ups and periods of remission and patients that require lifelong medical follow-up and treatment. The multiple intestinal and extraintestinal manifestations carry significant morbidity and significantly impacts the quality of life of the patients¹.

The 2 main subtypes are ulcerative colitis (UC) and Crohn disease (CD). UC colitis involves the colonic mucosa extending proximally from the anal verge in an uninterrupted pattern to involve all or part of the colon. In contrast CD is a transmural process with a specific predilection for small-bowel involvement. However, CD can occur anywhere in the gastrointestinal tract from mouth to anus, manifesting as patchy inflammation with intervening areas of normal mucosa but can also manifest with strictures and fistulas, each with varying symptom presentation and burdens. Still the cause remains elusive, although interplay of genetic, microbial and immunologic factors clearly exists^{1,2}.

Both diseases have a general commonality in their pathogenesis and are derived from a dysregulated or aberrant mucosal immune response to antigenic components of the normal commensal microbiota that reside within the intestine. They commonly present also with symptoms like rectal bleeding, stool frequency and bowel urgency (BU)^{2,3}.

Bowel urgency, the sudden or immediate need for a bowel movement, is distinct from increased stool frequency. It is one of the most bothersome symptoms experienced by patients with UC, with substantial negative impacts on patients' quality of life (QoL) and psychosocial functioning. Also, bowel urgency is one of the leading reasons patients with UC are displeased with their treatment and one of the symptoms most patients want improved. However, BU is often not discussed by patients due to embarrassment, and it may not be addressed adequately by healthcare providers (HCPs) due to a lack of awareness of validated tools and/or knowledge of the importance of assessing BU^{3,4,5}.

The underlying mechanisms of BU in patients with IBD are multifactorial and may vary within and between patient being driven primarily by active inflammation³.

Most patients, including those receiving treatment, experience urgency. In cross-sectional and observational

studies, more than 80% of patients reported bowel urgency³.

Evolving evidence suggests bowel urgency equally correlates with disease activity but also with the quality of life, psychological impact, clinical outcomes, and biomarkers.

In a survey of Japanese patients with ulcerative colitis, bowel urgency and bowel incontinence were associated with higher stool frequency and rectal bleeding scores, but BU also occurred in patients without frequent stools or rectal bleeding. When asked about the symptom they would most like to be improved, BU was the most common answer. Bowel urgency and the fear of urge incontinence were the most common reasons for patients declining participation in work, school, social, and physical activities³.

The management of chronic diseases such as IBD relies on strong patient-HCP relationships facilitated by good communication but frequently addressing bowel urgency during a medical visit is a challenge as both patients and physicians may not raise and discuss the topic^{5,6}.

Despite its impact on QoL and psychosocial function, bowel urgency is often neglected as a clinical symptom in UC patients. The mechanism of bowel urgency in UC is multifactorial, but the inflammatory component is responsive to treatment, so urgency might serve as a measure of insufficient disease control in active disease³.

Bowel urgency should be considered a third key PRO in UC in addition to rectal bleeding and stool frequency. Reduction in bowel urgency severity should be included in the definition of symptomatic and clinical remission and its evaluation and management can improve the QoL and treatment satisfaction of patients with IBD^{6,7,8}. To do this responsive and reliable patient-reported outcome measures of bowel urgency are needed to provide evidence of treatment benefits in clinical trials and facilitate communication in clinical practice^{5,6,7,8}.

MECHANISM DRIVING TO BOWEL URGENCY

The underlying mechanisms resulting in bowel urgency in patients with UC is unclear and probably multifactorial, including inflammatory changes of the rectum, hypersensitivity of the rectum, rectal contractile response/spasms, increased reactivity to rectal

distension, increased stool influx due to impaired colon function, and development of submucosal fibrosis associated with chronic inflammation causing decreased rectal wall compliance. Active inflammation is thought to be the principal cause of many symptoms.

Bowel motility can be accelerated with increased sigmoid-rectum transit because of an increase of propulsive pressure waves in this colonic segment. In addition, altered function of the rectal wall results in diminished distensibility, which reduces rectal capacity and leads to the arrival of fecal matter in an unaccommodated rectum. This generates increased pressure from smaller volumes and a subsequent sense of urgency.

Another mechanism for urgency is the anal sphincter “fatigability” which is higher in patients presenting with bowel urgency but is unrelated to local inflammation.

Anxiety and stress increase visceral sensitivity by the brain-gut axis, increasing the urgency feeling; this is a bidirectional system with interconnections between the neuroendocrine pathways, the autonomous nervous system and the gastrointestinal tract. Hypersensitivity is also associated with functional bowel disorders, which can occur alongside inflammatory bowel disease (IBD)³.

CLINICAL CONSIDERATIONS

Patients consider bowel urgency to be a more relevant and important symptom than abdominal pain, rectal bleeding, or stool frequency.

The CONFIDE study reported 45% and 37% of United States and European patients, respectively, with moderate-to-severe UC wore diapers, pads, or other protection at least once a week in the past 3 months for fear of a BU-related accident. The unpredictable and urgent nature of defecation, combined with uncertainty over access to facilities, increases the fear of having bowel “accidents” in public and may be as limiting as the actual incontinence. Bowel urgency is a key symptom for triggering clinical consideration of IBD diagnosis and for defining severity of disease activity in clinical practice³.

The assessment of bowel urgency is not a part of the frequently used activity indices and was not a recommended endpoint in clinical trials and real-world studies until recently; therefore, it was often overlooked during the past.

As it correlates with disease activity, QoL, psychological impact, clinical outcomes, and biomarkers,

absence of bowel urgency was strongly associated with improved clinical and endoscopic outcomes. The combination of bowel urgency, stool frequency, and blood in stool presence correlates with endoscopic findings and may be a surrogate marker for UC disease activity^{3,4,5}. Bowel urgency and urge incontinence are also associated with increased risk of colectomy, corticosteroid use and hospitalization.³

But also, patients may report bowel urgency even if they are considered in remission based on stool frequency, blood in stool scores and endoscopic findings.

This highlights the clinical relevance of bowel urgency and why dynamically assessing severity improvement over time versus a single yes/no time point metric is important. Health-care providers may assume they are addressing bowel urgency when other symptoms improve; however, in practice, approximately 35%–40% of patients with no rectal bleeding or normal stool frequency still have bowel urgency. Thus, bowel urgency remission may be an important goal independent of other symptoms and regardless of timing in relationship to other manifestations (3,6).

Dynamically monitoring patients’ urgency can be achieved with an index that includes bowel urgency as a relevant measure of disease activity such as the Simple Clinical Colitis Activity Index (SCCAI). For those HCP who use a UC index such as the SCCAI in their clinic, urgency is being asked about; however, often such indexes are not used clinically, and they can also be prone to bias if the clinician gives an interpretation of the patient’s response^{2,3}.

IMPACT ON PATIENTS’ LIFE

Over the last few decades, the study of QoL has received increasing interest from the medical research community, with a higher number of studies being published every year. Although neglected in the past, health-related quality of life (HR-QoL) has become one of the major endpoints of clinical studies. Patients with IBD have a lower HR-QoL compared to healthy individuals or the general population, with lower QoL scores in both the mental and physical domains.

Among patients with IBD, those with active disease have a significantly lower QoL compared to patients in remission. Patients with bowel urgency have reported feeling “trapped”, “dirty” and “lacking control”. Bowel urgency and the fear of urge incontinence were the most common reasons for patients declining participation in work/school, social, and physical activities.

The LISTEN 1 study found that bowel urgency and abdominal pain were rated the two most important symptoms in CD patients. BU was also the most important symptom in patients with UC, followed by stool frequency⁸. The CONFIDE study, which was a large-scale international survey found that up to half of patients with UC have experienced bowel urgency at least once a day and many of them not discussing this issue with their health care providers and the most common reason they avoided these discussions was embarrassment⁹.

The impact of inflammatory bowel disease (IBD) on sexual health is a leading concern among patients with most studies focus on sexual dysfunction rather than patient-perceived sexual quality of life (SQoL). Patients reported avoiding or decreased sexual activity due to UC in the last 3 months; bowel urgency and fear of BU-related accidents were two of the top three reasons. The emotional and self-esteem issues were the main concerns reported by IBD patients regarding sexual health which were strongly influenced by bowel urgency¹⁰.

Bowel urgency is associated with a higher risk of developing fatigue, regardless of severity and this close relationship between them highlights the need to address both during assessment and treatment. Fatigue is a common symptom in UC and is defined as an extreme, persistent sense of tiredness, weakness or exhaustion which is not easily resolved by sleep or rest².

HCP-PATIENT COMMUNICATION REGARDING BU

One of the key challenges highlighted in recent studies is the psychological discomfort the patients feel when discussing bowel urgency with their HCPs. The CONFIDE study revealed that BU was not perceived by the HCPs to be among the most common or important symptoms reported by patients. This study also revealed that embarrassment was the most common reason why patients avoided to discuss about the bowel urgency feeling. On the other hand, HCPs often did not proactively discuss bowel urgency, either due to insufficient time during appointments or because they expected the patient to bring it up. Other times patients may not report sensitive or embarrassing topics and HCPs may avoid sensitive topics due to not knowing how to address them. HCPs should actively probe concerns that patients may not initially feel comfortable discussing⁹.

A better communication and actively including and addressing bowel urgency into routine visit discussions with patients is a key for better care. The routine use of PROs during consultations can help clinicians improve medical care by better and more accurately evaluating the patients' needs^{4,5,7}.

BOWEL URGENCY ASSESSMENT

Bowel urgency is a key component of the Simple Clinical Colitis Activity Index. The SCCAI helps monitoring urgency and includes a question on bowel urgency using a four-point scale that lends itself to remote digital monitoring completed by patients. The ACG Ulcerative Colitis Activity Index and the Simple Clinical Colitis Activity Index for clinical evaluations include assessments of BU as a component³.

Several PRO tools have been developed, including the 29-item Symptoms and Impacts Questionnaire for Ulcerative Colitis, the Patient-Reported Outcome-Ulcerative Colitis diary, and the Urgency NRS^{3,11}.

The Urgency NRS is a single-item PRO measure that includes a 0 to 10 scale. It is easily understood by patients and has been confirmed by them to include appropriate response options, also has demonstrated construct validity and reliability¹¹.

A crosswalk analysis about treatment with mirikizumab response rates for 'absence/presence of urgency' using a binary questionnaire approximately correspond to scores ≤ 3 on the 11-point Urgency NRS, suggesting that a binary questionnaire may be insufficient to understand the degree of bowel urgency severity. Another benefit of UNRS is that it does not rely on specific descriptors that may have not been relevant to all patients due to the different and varied personal experiences of urgency^{11,12}.

TREATMENT IMPACT AND MONITORING

The management of bowel urgency can be challenging as there is limited evidence on the efficacy of therapies specifically for bowel urgency independent of IBD disease activity.

Most of the drugs currently used in IBD targets the inflammation characteristic of active disease. Treatment with upadacitinib, a Janus kinase inhibitor has been associated with significant improvements in BU alongside the achievement of clinical response and

remission¹³. Mirikizumab is a monoclonal antibody that inhibits anti-interleukin (IL)-23 by binding to an epitope on the p19 subunit. It is approved for the treatment of moderate to severe ulcerative colitis (UC) and is under development for Crohn disease and has demonstrated efficacy in reducing bowel urgency at week 12 versus those receiving placebo, and this improvement was sustained through week 52. Absence of bowel urgency was significantly associated with achievement of clinical response, clinical remission, Mayo stool frequency remission, Mayo rectal bleeding remission, Mayo endoscopic remission, histologic remission, and mucosal healing at weeks 12 and 52. Mirikizumab has also been demonstrated as an acceptable safety profile in patients with moderate to severe CD that was consistent with the known safety profile in patients with moderate to severe UC^{14,15}. In the VIVID-1 study, results from phase 3 revealed that remission were not statistically different for mirikizumab and ustekinumab. However, mirikizumab showed numerically superior results for the endpoints. Another result is that mirikizumab reached nominal statistical superiority to ustekinumab in decreasing fecal calprotectin and C reactive protein^{12,14,15}.

The phase 3 INSPIRE study evaluated induction therapy with risankizumab (IL-23 inhibitor) vs placebo in patients with moderately to severely active UC and significantly improved abdominal pain, bowel urgency and fecal incontinence¹⁶.

Bowel urgency caused by inflammatory and non-inflammatory mechanisms might be improved also with antidiarrheal agents like loperamide^{3,13}. Other measures include avoiding triggering foods, improving hygiene, reducing fiber and caffeine intake especially after meals, because it stimulates motility of the colon.^{3,13}

CONCLUSIONS

Bowel urgency, the sudden or immediate need for a bowel movement, is distinct from increased stool frequency. It is one of the most bothersome symptoms experienced by patients with UC, with substantial negative impacts on quality of life (QoL) and psychosocial functioning.

The underlying mechanisms resulting in bowel urgency in patients with UC are unclear and probably multifactorial. Absence of bowel urgency was strongly associated with improved clinical and endoscopic outcomes, lower levels of biomarkers such as fecal

calprotectin and high-sensitivity C-reactive protein (hs-CRP).

A better communication and actively including and addressing bowel urgency into routine visit discussions with patients is a key for better care. The routine use of PROs during consultations can help clinicians improve medical care by better and more accurately evaluating the patients' needs.

The management of bowel urgency can be challenging but recent studies showed increased efficacy from mirikizumab, upadacitinib and risankizumab.

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